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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,674	10/25/2001	Robert C. Ladner	D2033-708931	2458
37462 7590 10/05/2010 LANDO & ANASTASI, LLP ONE MAIN STREET, SUITE 1100 CAMBRIDGE, MA 02142				
EXAMINER				
BOESEN, CHRISTIAN C				
ART UNIT		PAPER NUMBER		
1639				
NOTIFICATION DATE		DELIVERY MODE		
10/05/2010		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@LALaw.com  
gengelso@LALaw.com

# Office Action Summary

**Application No.**

10/045,674

**Applicant(s)**

LADNER ET AL.

**Examiner**

CHRISTIAN BOESEN

**Art Unit**

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 April 2009.  
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 227-234, 240, 243 and 248-262 is/are pending in the application.  
4a) Of the above claim(s) 248-262 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 227-234, 240 and 243 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)  
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 08/07/2008, 09/05/2008, 11/07/2008, 04/08/2009, 11/04/2009, 02/04/2010 and 06/04/2010  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_  
5) ☐ Notice of Informal Patent Application  
6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This Non-Final Office Action is responsive to the communication received 04/30/2009.

#### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/30/2009 has been entered.

#### ***Claim Status***

Claim(s) 1-226, 235-239, 241-242 and 244-247 have been canceled as filed on 04/30/2009.

Claim(s) 227 have been amended as filed on 04/30/2009.

Claim(s) 227-234, 240, 243 and 248-262 are currently pending.

Claim(s) 248-262 have been withdrawn.

Claim(s) 227-234, 240 and 243 are being examined in this application.

#### ***Election/Restrictions***

Applicant's election with traverse in the reply filed on 04/26/2005 of group IV, claims 227-234, 240 and 243 is noted. New/amended claim(s) 227 are grouped with the elected group IV invention.

Discussion and Answer to Argument

Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Applicant argues that claims 248-262 should be examined because claims 248-262 properly limit examined claims of the group IV invention.

In response to Applicant's arguments, the Examiner respectfully disagrees. The restriction of 02/28/2005 contained five groups, three of which were drawn to products: Group III a library of genetic packages, Group IV a library of a collection of members of a diverse family of peptides and Group V a nucleic acid vector. The Applicant elected Group IV and later submitted new claims 248-262 that fall within non-elected groups III or V. Thus, claims 248-262 are not in the elected Group IV and are not examined.

Applicant's argument would be true if "dependent" claims 248-262 actually provided some further limitation for the subject matter in claims 227-234, 240, and 243. However, this is not the case (i.e., these claims were improperly listed as dependent claims). Thus, Applicant's argument is moot. Furthermore, even if, assuming *arguendo*, claims 248-262 did further limit claims 227-234, 240 and 243 (which is not the case), Applicant elected a library of proteins, not a library of protein-linkers or a library phage particles and. As discussed in the restriction, a search for Applicant's elected proteins would not necessarily turn up art for the protein-linkers or phage particles set forth in withdrawn claims 249-262. For example, the elected proteins could be located in journals drawn to solid-phase peptide synthesis rather than phage display. In addition, the peptides can be separately classified and thus would require a separate burdensome classification search (e.g., see class 510, subclass 810 wherein peptides bound to a solid support

are set forth; see also class 530, subclass 350 for peptides that are not bound to a solid-support; see also class 424, subclass 192.1 wherein “fusion proteins” like the ones used in phage display are set forth; compare also class 506, subclass 14 to class 506, subclass 18 wherein a “displayed” library such as a library of phage particles is classified separately from a library proteins that are not displayed). Here, Applicant elected a library of peptides, polypeptides, or proteins that were not displayed (i.e., classified in 506, subclass 18) rather than a library that is displayed on a phage with the use of a linker (e.g., see class 506, subclass 14). This can be clearly seen from Applicant's election of Group IV (i.e., library of peptides, proteins, etc.) rather than Group III (i.e., a phage library).

Claim 249 reads, “wherein the diversity of peptides, polypeptides or proteins is displayed on genetic packages.” Original claim 11, drawn to non-elected Group III reads, “A library comprising a collection of genetic packages that display a member of a diverse family of peptides, polypeptides or proteins ....” The Examiner fails to see the difference. That is reversing the subject/verb order does not change the meaning of the claim. Writing a claim drawn a diversity of peptides that is “displayed” on a collection of genetic packages is exactly the same as writing a claim drawn to a collection of genetic packages that display the diversity of peptides. Claim 248, for example, doesn't state that the library of peptides have been “cleaved” from the genetic packages. Furthermore, a phage (an the fusion peptides expressed thereon) doesn't further limit a peptide as erroneously purported by Applicant and even if did (which is not the case, see above) it would be withdrawn from consideration as drawn to non-elected subject matter as a result of the divergent subject matter and burdensome search.

***Priority***

This application for patent is filed under 35 U.S.C. 111(a) of 10/045,674 (filed on 10/25/2001).

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(e) is acknowledged. Acknowledgment is made for priority to a CIP application 10/000,516 (filed on 10/24/2001), a CIP application 09/837,306 (filed on 04/17/2001) and a provisional application 60/198069 (filed on 04/17/2000).

***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on 08/07/2008, 09/05/2008, 11/07/2008, 04/08/2009, 11/09/2009, 02/04/2010 and 06/24/2010 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the Examiner.

***Previous Rejections and/or Objections***

Any objections and/or rejections raised in the previous Office Action but not reiterated below are considered to have been withdrawn in view of the Applicant's amendments filed on 04/30/2009.

***New Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

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Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

**Claims 227-234, 240 and 243 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.**

**Claim 227** is drawn to a library of peptides, polypeptides or proteins, wherein the peptides, polypeptides or proteins each comprise a VH CDR1 and a VH CDR2. A polypeptide containing a VH CDR1 and a VH CDR2 is not an art recognized term. A polypeptide containing a VH CDR1 (e.g., SEQ ID NO 636) and a VH CDR2 (e.g., SEQ ID NO 637) is effectively a random set of expressed amino acid residues that has no known utility. If Applicants instead intend the product to be a library of antibodies an amendment of "the antibodies or antibody fragments each comprise a VH CDR1 and a VH CDR2" would overcome this rejection.

***New Claim Rejections - 35 USC § 112 - 2nd paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 227-234, 240 and 243 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

**Claim 227** is indefinite for reciting the phrase "the peptides, polypeptides or proteins each comprise a VH CDR1 and a VH CDR2" because one of ordinary skill in the art could not reasonably determine the metes and bounds of this limitation. The instant term does

not appear to be an established term in the art, but rather a term that applicants are using to categorize certain antibodies. An amendment of "the antibodies or antibody fragments each comprise a VH CDR1 and a VH CDR2" would overcome this rejection.

***Claim Rejections - 35 USC § 103 - Necessitated by Amendment***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
5. Secondary considerations (objective evidence of nonobviousness): a) commercial success; b) long felt need; c) evidence of unexpected results; d) skepticism of experts; and e) copying.

Claims 227-234, 240 and 243 are obvious over Pini in view of Stewart and Yang as evidenced by Tomlinson and Brezinschek:

**Claims 227-234, 240 and 243 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pini (08/21/1998) Journal of Biological Chemistry volume 273 pages 21769 to 21776 in view of Stewart (02/01/1993) Journal of Experimental Medicine volume 177 pages 409 to 418 and Yang (1995) Journal of Molecular Biology volume 254 pages 392**



**to 403 as evidenced by Tomlinson (10/05/1992) Journal of Molecular Biology volume 227 pages 776 to 798 and Brezinschek (05/1997) Journal of Clinical Investigation volume 99 pages 2488 to 2501. This rejection is necessitated by Applicant's amendatory material of "comprising ... the ... SEQ ID NO" to claim 227.**

Applicant's claimed invention is broad and is generally directed to a library of polypeptides that include portions related to antibody regions VH CDR1 and VH CDR2 sequences. The Applicant's invention involves the specific sequences -X<sub>1</sub>-Y-X<sub>2</sub>-M-X<sub>3</sub>- (SEQ ID NO:636) and X<sub>4</sub>-I-X<sub>5</sub>-X<sub>6</sub>-S-G-G-X<sub>7</sub>-T-X<sub>8</sub>-Y-A-D-S-V-K-G- (SEQ ID NO:637), and may also contain VH CDR3, VH 3-23 framework regions and an antibody light chain. Claim 227 recites:

"A library comprising a collection of members of a family, the family comprising a diversity of peptides, polypeptides or proteins, wherein the peptides, polypeptides or proteins each comprise a VH CDR1 and a VH CDR2 and are encoded by DNA sequences comprising sequences encoding (a) the VH CDR1, wherein the VH CDR1 comprises the amino acid sequence according to the formula -X<sub>1</sub>-Y-X<sub>2</sub>-M-X<sub>3</sub>- (SEQ ID NO:636), wherein X<sub>1</sub>, X<sub>2</sub>, and X<sub>3</sub> are independently selected from the group consisting of A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, and Y, and (b) the VH CDR2, wherein the VH CDR2 comprises the amino acid sequence according to the formula X<sub>4</sub>-I-X<sub>5</sub>-X<sub>6</sub>-S-G-G-X<sub>7</sub>-T-X<sub>8</sub>-Y-A-D-S-V-K-G- (SEQ ID NO:637), wherein X<sub>4</sub> and X<sub>5</sub> are independently selected from the group consisting of Y, R, W, V, G, and S, X<sub>6</sub> is selected from the group consisting of P and S, and X<sub>7</sub> and X<sub>8</sub> are independently selected from the group consisting of A, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W, and Y."

Regarding **claims 229 and 231-233** are product-by-process claims and the process recited in this claim is not given any patentable weight. See MPEP 2113, "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which

reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith."

With regards to **claim 227**, Pini and Stewart teach SEQ ID NO 636 (e.g., VH CDR1) (see results 16, 1 and 53 below and Pini as evidenced by Tomlinson e.g., antibody DP-47, see Figure 2b). Compared to SEQ ID NO 637 (e.g., VH CDR2) Pini teaches differences are  $X_4 = A$  and  $X_6 = G$  (e.g., underlined in result 16 below) and Pini teaches the difference is the first  $G = S$  (e.g., clones H10 and L19, see Pini, Table II positions 50 and 52). Steward teaches the difference is  $X_6 = G$  (e.g., underlined in result 1 below) and Steward teaches differences are the first  $G = S$  and  $T = I$  (e.g., underlined in result 53 below), thus, in five sequences containing SEQ ID NO 636 and sequences similar to SEQ ID NO 637 Pini and Stewart teach that in VH CDR2  $X_4$  can be A, S, G or Y and  $X_6$  can be G or S meeting the claim limitations of  $X_4$  and  $X_6$  in SEQ ID NO 637. Wang teaches saturation mutagenesis of antibody CDRs including VH CDR1 and VH CDR2 (see Abstract).

This page gives you Search Results detail for the Application 10045674 and Search Result 20100916\_173349\_us-10-045-674d-63614x637.rup.

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GenCore version 6.3  
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OM protein - protein search, using sw model

Art Unit: 1639

Run on: September 16, 2010, 18:21:31 ; Search time 79 Seconds  
(without alignments)  
1722.987 Million cell updates/sec

Title: US-10-045-674D-63614X637

Perfect score: 95

Sequence: 1 **XYXXXXXXXXXXXXXXXXXXXXXSGGXTXYADSVKG 36**

Scoring table: BLOSUM62DX  
Gapop 10.0 , Gapext 0.1

Searched: 11627486 seqs, 3757527982 residues

Total number of hits satisfying chosen parameters: 11627486

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 150 summaries

Database : UniProt\_201006:\*  
1: uniprot\_sprot:\*  
2: uniprot\_trembl:\*  
SUMMARIES

Result No.	Score	% Query		DB	ID	Description
		Match	Length			
1	95	100.0	90	2	<b>A2NWX0_HUMAN</b>	<b>A2nwx0 SubName: Fu</b>
2	95	100.0	99	2	A2NWX8_HUMAN	A2nwx8 SubName: Fu
3	95	100.0	100	2	A2NWX7_HUMAN	A2nwx7 SubName: Fu
4	95	100.0	101	2	A2NWX6_HUMAN	A2nwx6 SubName: Fu
5	95	100.0	103	2	A2NWX9_HUMAN	A2nwx9 SubName: Fu
6	95	100.0	105	2	A2NWX4_HUMAN	A2nwx4 SubName: Fu
7	95	100.0	106	2	A2NWX5_HUMAN	A2nwx5 SubName: Fu
8	95	100.0	106	2	A2NWX1_HUMAN	A2nwx1 SubName: Fu
9	95	100.0	110	2	A2NWX2_HUMAN	A2nwx2 SubName: Fu
10	95	100.0	110	2	A2NWX3_HUMAN	A2nwx3 SubName: Fu
11	95	100.0	111	2	A2NWX2_HUMAN	A2nwx2 SubName: Fu
12	95	100.0	113	2	A2NWX1_HUMAN	A2nwx1 SubName: Fu
13	95	100.0	121	2	A2KUC3_HUMAN	A2kuc3 SubName: Fu
14	95	100.0	131	2	A2NZ55_HUMAN	A2nz55 SubName: Fu
15	95	100.0	161	2	A2NUT3_HUMAN	A2nut3 SubName: Fu
16	95	100.0	238	2	<b>A2KBB9_HUMAN</b>	<b>A2kbb9 SubName: Fu</b>
17	95	100.0	238	2	A2KBC2_HUMAN	A2kbc2 SubName: Fu
18	95	100.0	238	2	A2KBC3_HUMAN	A2kbc3 SubName: Fu
19	95	100.0	238	2	A2KBC4_HUMAN	A2kbc4 SubName: Fu
20	95	100.0	238	2	A2KBC5_HUMAN	A2kbc5 SubName: Fu
21	95	100.0	238	2	A2KBC6_HUMAN	A2kbc6 SubName: Fu
22	95	100.0	238	2	A2KBC7_HUMAN	A2kbc7 SubName: Fu
23	95	100.0	238	2	A2KBC8_HUMAN	A2kbc8 SubName: Fu
24	95	100.0	244	2	A2J422_HUMAN	A2j422 SubName: Fu
25	92	96.8	112	2	Q9HCC1_HUMAN	Q9hcc1 SubName: Fu
26	91	95.8	117	1	HV303_HUMAN	P01764 RecName: Fu
27	91	95.8	121	2	Q9UL71_HUMAN	Q9ul71 SubName: Fu
28	91	95.8	584	2	Q6INK3_XENLA	Q6ink3 SubName: Fu
29	91	95.8	589	2	Q5XHD5_XENLA	Q5xhd5 SubName: Fu
30	91	95.8	593	2	Q6INM5_XENLA	Q6inm5 SubName: Fu

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31	90	94.7	96	2	D2I8G8_AILME	D2I8g8	SubName: Fu
32	87	91.6	117	2	D3ZJW6_RAT	D3zjw6	SubName: Fu
33	87	91.6	120	1	HV32I_HUMAN	P01782	RecName: Fu
34	87	91.6	128	2	A2KD62_LAMGL	A2kd62	SubName: Fu
35	87	91.6	128	2	A2KD64_LAMGL	A2kd64	SubName: Fu
36	86	90.5	98	2	A2JLN2_HUMAN	A2jln2	SubName: Fu
37	86	90.5	117	2	A2NTS3_MOUSE	A2nts3	SubName: Fu
38	86	90.5	117	2	D3ZF20_RAT	D3zf20	SubName: Fu
39	86	90.5	118	2	D3ZE00_RAT	D3ze00	SubName: Fu
40	86	90.5	118	2	D4A6W2_RAT	D4a6w2	SubName: Fu
41	86	90.5	120	2	D3ZIT2_RAT	D3zit2	SubName: Fu
42	86	90.5	136	2	D4ACV5_RAT	D4acv5	SubName: Fu
43	86	90.5	138	2	A2NV20_MOUSE	A2nv20	SubName: Fu
44	86	90.5	467	2	Q4VBH1_RAT	Q4vbh1	SubName: Fu
45	86	90.5	475	2	Q6MEQ6_HUMAN	Q6mez6	SubName: Fu
46	85	89.5	77	2	D2I8T8_AILME	D2I8t8	SubName: Fu
47	85	89.5	109	2	D2I8H4_AILME	D2I8h4	SubName: Fu
48	85	89.5	128	2	A2KD63_LAMGL	A2kd63	SubName: Fu
49	85	89.5	236	2	A2KBC1_HUMAN	A2kbc1	SubName: Fu
50	85	89.5	238	2	A2KBC0_HUMAN	A2kbc0	SubName: Fu
51	85	89.5	470	2	Q68CN4_MOUSE	Q68cn4	SubName: Fu
52	84	88.4	117	1	HVM524_MOUSE	P18524	RecName: Fu
53	83	87.4	97	2	A2NWX4_HUMAN	A2nwx4	SubName: Fu

**RESULT 16**

A2KBB9\_HUMAN

ID A2KBB9\_HUMAN Unreviewed; 238 AA.  
AC A2KBB9;  
DT 20-FEB-2007, integrated into UniProtKB/TrEMBL.  
DT 20-FEB-2007, sequence version 1.  
DT 02-MAR-2010, entry version 13.  
DE SubName: Full=Anti-(ED-B) scFv;  
DE Flags: Fragment;  
OS Homo sapiens (Human).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;  
OC Catarrhini; Hominidae; Homo.  
OX NCBI\_TaxID=9606;  
RN [1]  
RP NUCLEOTIDE SEQUENCE.  
RX MEDLINE=98371014; PubMed=9705314; DOI=10.1074/jbc.273.34.21769;  
RA Pini A., Viti F., Santucci A., Carnemolla B., Zardi L., Neri P.,  
RA Neri D.;  
RT "Design and use of a phage display library. Human antibodies with  
RT subnanomolar affinity against a marker of angiogenesis eluted from a  
RT two-dimensional gel.";  
RL J. Biol. Chem. 273:21769-21776(1998).  
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CC -----  
DR EMBL; AJ006111; CAA06862.1; -; mRNA.  
DR IPI; IPI00916434; -.  
DR UniGene; Hs.510635; -.  
DR UniGene; Hs.703932; -.  
DR SMR; A2KBB9; 1-238.  
DR STRING; A2KBB9; -.  
DR HOVERGEN; HBG005814; -.







One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in arriving at the Applicant's invention as claimed with the above cited references before them. Pini, Stewart and Yang are directed towards libraries of antibody polypeptides that include portions related to antibody regions VH CDR1 and VH CDR2 sequences. Pini and Stewart teach libraries that include polypeptides that code for -X<sub>1</sub>-Y-X<sub>2</sub>-M-X<sub>3</sub>- in the VH CDR1 region and a VH CDR2 region that is almost identical to SEQ ID NO 637. Pini and Stewart teach in VH CDR2 X<sub>4</sub> can be A, G or Y and X<sub>6</sub> can be G or S meeting the claim limitation of X<sub>4</sub> is Y, R, W, V, G or S and X<sub>6</sub> is P or S. One of ordinary skill in the art would have recognized the advantages of using the approach of varying X<sub>4</sub> and X<sub>6</sub> to other residues from known antibodies because Yang teaches that saturation mutagenesis of CDRs, including VH CDR2, can result in an improvement in antibody affinity (see Abstract). Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

***Common Ownership of Claimed Invention Presumed***

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).



***Conclusion***

No claim is allowed.

If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (e.g., if the amendment is not supported *in ipsi verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to CHRISTIAN BOESEN whose telephone number is 571-270-1321. The Examiner can normally be reached on Monday-Friday 9:00 AM to 5:00 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher S. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christian Boesen/  
Examiner, Art Unit 1639

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